

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference BSCI00801WO	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2005/010146	International filing date (day/month/year) 29/03/2005	(Earliest) Priority Date (day/month/year) 30/03/2004
Applicant BOSTON SCIENTIFIC SCIMED, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 05 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

FIG 1AS /PCT Search Report
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DUE: 26 AUG 2005 26 AUG 2005
EOL: 26 OCT 2005 26 OCT 2005

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JUL 29 2005

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5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

/US2005/010146

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61K35/28 A61P9/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TANG Y L ET AL: "Autologous mesenchymal stem cell transplantation induce VEGF and neovascularization in ischemic myocardium" REGULATORY PEPTIDES 15 JAN 2004 NETHERLANDS, vol. 117, no. 1, 15 January 2004 (2004-01-15), pages 3-10, XP002333008 ISSN: 0167-0115 page 3, right-hand column page 6, left-hand column, paragraph 3 - right-hand column, paragraph 2 page 9, left-hand column, paragraph 3 - right-hand column, paragraph 1</p> <p>----- -/--</p>	<p>1-7,9, 10, 13-16, 18,19</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

12 July 2005

Date of mailing of the international search report

26/07/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Escolar Blasco, P

INTERNATIONAL SEARCH REPORT

International Application No

/US2005/010146

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WALTERS DARREN L ET AL: "Acute coronary syndrome is a common clinical presentation of in-stent restenosis" AMERICAN JOURNAL OF CARDIOLOGY, vol. 89, no. 5, 1 March 2002 (2002-03-01), pages 491-494, XP002333023 ISSN: 0002-9149 abstract -----	1-21
X	WO 00/06701 A (GENZYME CORPORATION) 10 February 2000 (2000-02-10) page 26, lines 10-20 page 21, lines 8-15; claims 1-11 -----	1-5, 9-12
A	WO 03/073998 A (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM; STUDENY, MATUS; ANDR) 12 September 2003 (2003-09-12) page 44, line 7 -----	1-21
A	WERNER NIKOS ET AL: "Intravenous transfusion of endothelial progenitor cells reduces neointima formation after vascular injury." CIRCULATION RESEARCH. 25 JUL 2003, vol. 93, no. 2, 25 July 2003 (2003-07-25), pages e17-e24, XP002333009 ISSN: 1524-4571 page 22, right-hand column, paragraph 2 -----	1-14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/010146

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 1-21: Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2005/010146

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0006701	A	10-02-2000	AU 5545499 A	21-02-2000
			BR 9912662 A	05-06-2001
			CA 2339182 A1	10-02-2000
			EP 1100870 A1	23-05-2001
			JP 2002521493 T	16-07-2002
			WO 0006701 A1	10-02-2000
			US 2005031600 A1	10-02-2005
WO 03073998	A	12-09-2003	AU 2003213666 A1	16-09-2003
			CA 2477411 A1	12-09-2003
			EP 1487463 A2	22-12-2004
			WO 03073998 A2	12-09-2003
			US 2004076622 A1	22-04-2004

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2005/010146

International filing date (day/month/year)
29.03.2005

Priority date (day/month/year)
30.03.2004

International Patent Classification (IPC) or both national classification and IPC
A61K35/28, A61P9/10

Applicant
BOSTON SCIENTIFIC SCIMED, INC.

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1. This opinion contains indications relating to the following items:

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- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Resp + written opinion
ENTERED
DUE: 30 DE 2005
EOL: 30 JA 2006

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Escobar Blasco, P

Telephone No. +49 89 2399-7331



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/010146

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/010146

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-21, in respect of IA

because:

- ☒ the said international application, or the said claims Nos. 1-21 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2005/010146

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	8,11-21
	No: Claims	1-7,9,10
Inventive step (IS)	Yes: Claims	
	No: Claims	1-21
Industrial applicability (IA)	Yes: Claims	see separate sheet
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Comments on item III

Claims 1-21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Comments on item V

1. Reference is made to the following documents cited in the International Search Report. Any reference to the documents in the present written opinion relates to the passages given in said report, unless otherwise indicated.

D1: TANG Y L ET AL: "Autologous mesenchymal stem cell transplantation induce VEGF and neovascularization in ischemic myocardium" REGULATORY PEPTIDES 15 JAN 2004 NETHERLANDS, vol. 117, no. 1, 15 January 2004, pages 3-10

D2: WALTERS DARREN L ET AL: "Acute coronary syndrome is a common clinical presentation of in-stent restenosis" AMERICAN JOURNAL OF CARDIOLOGY, vol. 89, no. 5, 1 March 2002, pages 491-494

D3: WO 00/06701 A

D1: WO 03/073998 A

2. D1 and D3 relate to the administration of mesenchymal stem cells (MSC) to patients with ischemic heart diseases. These patients are often treated with transluminal angioplasty and are at risk of developing restenosis (see in addition D2, which explains that patients with restenosis present often symptoms of coronary artery disease). These documents anticipate thus the subject-matter of claims 1-5 and 9-10 due to the broad expressions "patient at risk for developing restenosis" and "vascular trauma".

- 2.1 D1 anticipates the subject-matter of claims 6-7 as well.

3. The subject-matter of claims 8, 11 and 12 has not been disclosed in any of the available documents. However, said claims contain technical features which appear to be customary in the art. Considering that no unexpected effect is cited in the present description in relation to these features, no inventive step can be acknowledged at present.
4. The subject-matter of claims 13-21 is considered as formally novel over the prior art. However, it cannot be regarded as inventive for the following reasons:
D4 relates to therapeutic uses of MSC and cites restenosis among other conditions. The present application differs from D4 in that restenosis is specifically selected as medical indication of MSCs.
But in the present case it is considered that no problem has been actually solved, as the data in the description relates to experiments to be done (but apparently not yet carried out). Hence, it is not known yet whether the choice of restenosis really solves the problem of providing a further medical use of MSCs.
5. For the assessment of the present claims 1-21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Comments on item VII

Claims 5 and 14 lack clarity, since an inflammatory response is normally produced by the body, and not administered to it.